RECORD OF ORAL HEARING

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte JENNIFER L. SCHMITKE,
DONGHAO CHEN, RICHARD P. BATYCKY,
DAVID A. EDWARDS, and JEFFREY S. HKRACH

Appeal 2007-0913
Application 09/888,126
Technology Center 1600

Oral Hearing Held: June 5, 2007

Before DONALD E. ADAMS, LORA M. GREEN, and NANCY J. LINCK,
Administrative Patent Judges

APPEARANCE:

ON BEHALF OF THE APPELLANTS:

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Victoria Gudemen, Reporter

JUDGE ADAMS: Good morning.

MS. ELMORE: Good morning.

JUDGE ADAMS: Now you may begin. And if you could start by introducing your associate or associates and --

MS. ELMORE: This is Donna Ward. She works with me --

JUDGE ADAMS: Um-hum.

MS. ELMORE: -- at Elmore Patent Law Group. I'm accompanied by Paula Davis -- whose the Licensee of the patent applications under appeal. And Kathy Beaverstien, who's a general counsel --

JUDGE ADAMS: Great. Good morning. We have a number of examiners from 3700, is that right? Thirty-six. Excuse me, 3600. And we're familiar with your case. You have 20 minutes and you can start when you're ready.

MS. ELMORE: Terrific. We actually have two appeals this morning.

JUDGE ADAMS: Okay.

MS. ELMORE: And if it's acceptable to you, I would like to start with the 0193 appeal.

The primary issue on appeal in this case, I believe, is whether the data of records -- assuming a prima facie case has been made. It became clear, as I was reviewing the data with my colleagues, that -- in preparation for this meeting, that the data may not have been presented in as a clear and concise a fashion as it could've been. And if I may, I would like to present to you a table format of declaration evidence.

JUDGE ADAMS: We'll use that just for today and we'll give that back to you.

MS. ELMORE: That would be fine.

JUDGE ADAMS: I take it that examiner hasn't seen it yet. And this is the data that's in the declaration, is that right?

MS. ELMORE: This is the data that's in the declaration as just presented and I worked with a different format, so I had to review it and present it Figure 4. It's presented as in patentable form. The table describes the amount of each solid which is in the solution --

JUDGE ADAMS: Um-hum.

MS. ELMORE: -- of the formulation as it's being produced. So the claimed invention is directed to a formulation comprising 60 percent dipalmitoylphosphatidylcholine [DPPC], 30 percent insulin and 10 percent sodium citrate. Those ingredients are combined into -- water solution for manufacturing and are then spray dried. This table -- the data --

COURT REPORTER: Excuse me. I'm sorry.

(Pause.)

COURT REPORTER: Thank you.

MS. ELMORE: Sure. The data in the declaration is directed to the solubility for the period of time that each solution, after it's made, precipitates or what we call crashes out.

JUDGE ADAMS: And this would be -- this, of course, would belong to Figure 2 in the declaration?

MS. ELMORE: Figures 1 and 2 both provide that data in different -- in different presentations.

JUDGE ADAMS: And the idea of the crash-out is just basically the amount of time it takes for a certain concentration of insulin to fall out of solution, is that right?

MS. ELMORE: Not just the insulin, but all of the solutes --

JUDGE ADAMS: Okay.

MS. ELMORE: -- so the insulin --

JUDGE ADAMS: Thank you.

MS. ELMORE: Okay?

JUDGE ADAMS: Um-hum.

MS. ELMORE: As one would expect as you increase the amount of solutes in a solution, one would expect that the solutes would precipitate -- generally precipitate out of the solution faster. That's the conventional, conventional wisdom or expectations in a normal, in a normal situation.

What we discovered with this specific formulation or combination of excipients in insulin was that by increasing the amount of insulin, we could put more total solutes into solution and either delay or prolong the crash-out period. And this is really what was the unexpected result.

For example, if you look at -- so on this table, Column -- Row A is the claimed invention. Rows B, C and D are the comparators of the invention. And if you compare -- look at Column D-3, which has -- describes a solution made of 80 percent DPPC or 12 grams per liter of the lipid, one-and-a-half grams per liter of insulin, and one-and-a-half grams of citrate -- that solution crashed-out were precipitated in five minutes after mixing.

In contrast, A-4, which is the claimed, the claimed formulation at 20 grams per liter -- so five grams per liter more total solutes -- contained the same amount of lipid, 12 grams per liter; four times the amount of insulin, six grams per liter; and slightly more citrate, two grams per liter. Unexpectedly, by increasing the insulin concentration, this solution didn't crash out for 20 minutes as compared to five, and this was truly an unexpected result.

The amount of insulin added was not insignificant. Again, we increased fourfold the amount of insulin, for an additional four-and-a-half grams of protein. Considering the total amount of solutes, 20 grams per liter, this was -- this is a significant amount.

The result can be seen throughout the table. For example, the protecting properties of the increased insulin concentration can be seen by comparing A-2, which is the same formulation concentration of 10 grams per liter; and D-1, which contains less DPPC, less insulin and less citrate and crashed out in a third of the time.

The advantage of the invention is that the -- when you go to make the formulation, you don't need to worry about how quickly the formulation runs from first mixing through the spray dryer, so you get a better quality of result more consistently. So with the D-3 formulation, for example, you need to -- at 15 grams per liter, which is the actual concentration that we used in manufacturing this product, the formulation would mean consistently get from mixing through the spray dryer within five minutes.

JUDGE ADAMS: Which one of these formulations corresponds to the closest prior art in this case?

MS. ELMORE: We believe that the -- that the comparisons presented are closer than the prior art cited by the examiner. The rejection was on the combination of Patton and Edwards.

JUDGE ADAMS: Um-hum.

MS. ELMORE: Patton differs from the claimed invention, in that it doesn't have DPPC at all. It describes formulations which contain insulin and citrate and insulin, a sugar or carbohydrates, such as raffinose and mannitol and citrate. Edwards describes products which have insulin, DPPC and carbohydrates. What this, what this comparison does -- the rejection relies upon two fundamental modifications. One is the selection of excipients from two generic teachings. There's no specific teaching in the prior art of this specific combination of insulin, DPPC and citrate.

The second fundamental modification that the examiner relies upon in the rejection is the selection of the specific amounts of the three components. What this comparison does is it assumes that the first modification alleged by the examiner is correct, that the selection of those three specific excipients is obvious, and it shows that the identification or the selection of the specific amounts of those three components resulted in unobvious properties. So we believe that this is an indirect comparison and we have compared a formulation which is closer than the prior art.

JUDGE LINCK: The patent discloses formulations with 20 percent insulin. How do we know that what you've done here is any better than Patton's formulations, other than you've just substituted one of the excipients?

MS. ELMORE: Patton's formulation, though, relies -- the rejection fundamentally requires that you add DPPC. So in looking at the -- at the Patton formulation, one needs to add the DPPC. The Patton formulation is made by spray drying in baking solution. DPPC is not soluble in a baking solution at all. It's not -- the comparison of the Patton formulation would not be appropriate because it doesn't -- it would require more modifications to run the comparison than what we have compared.

JUDGE LINCK: But if you just substituted DPPC or raffinose or mannitol and you've gotten the same results, that's a single substitution. Is that really a patentable invention?

MS. ELMORE: Well, we actually need to have two substitutions because the claims are directed for a 60/30/10 formulation. Patteo describes raffinose concentration or a mannitol concentration of 66 percent, 20 percent insulin and 12 percent citrate. You still need to make that modification in the concentration even if you just simply switched the lipid and the mannitol or the lipid and raffinose. Because this lipid, dipalmitoylphosphatidylcholine, is not soluble in water, we couldn't just simply substitute DPPC with raffinose because the formulation wouldn't go into solution at all. The introduction of ethanol is required. And so at that point in time we felt that in presenting a comparison, that we compared what was closer, because we made the modifications -- be necessary in order to make the modification alleged by the examiner.

JUDGE ADAMS: Well, it seems to be what's driving this is the concentration of insulin, is that right?

MS. ELMORE: That's correct.

JUDGE ADAMS: So in Formulation B, according to your table, you have an insulin concentration of 20 percent total solid, is that right?

MS. ELMORE: Um-hum.

JUDGE ADAMS: Would that be comparative to the prior art -- 20 percent formulation -- a formulation that comprises 20 percent insulin, is that right?

MS. ELMORE: That would be comparable.

JUDGE ADAMS: Okay. And if we move across to 20 grams per liter in Formulation D --

MS. ELMORE: Um-hum.

JUDGE ADAMS: -- the concentration of insulin relative to the total solid is 20 percent and that corresponds to the prior art. Insulin is what's driving this reaction, this fall out time, and we have a crash-out of 20 minutes, which corresponds to your formulation, is that right?

MS. ELMORE: Well -- so if you look only at the isolated data points and data point in View 4, you are correct. Both of those formulations at the same concentration crash-out at the same time. But if you compare A-2 and B-2, you'll see that -- that the insulin at 10 grams per liter did have a substantial impact on the solubility. We were able to increase -- we were able double the increase from five grams per liter of concentration to 10 grams per liter, increase the amount of lipid in the solution, and triple the amount of insulin and double the amount of citrate.

Similarly, in comparing, for example, A-3 and B-2, we increased the amount of DPPC from seven to nine, more than doubled the amount of insulin from two to four and a half, and increased the amount of

citrate, yet had a modest increase in the crash-out time. So while you're correct, if you look at one data point of A-4 and B-4, you don't see a substantial difference. However, there is a significant difference across the table as a whole, which I believe supports the argument that there's something special about the 60/30/10 formulation.

In accordance -- this situation is not like the -- what -- the situation before In re Chupp. If you compare our formulation with the herbicide that was being -- that was the subject of the claims in Chupp, and you use of the formulation in multiple concentrations and solubility environments, while it may be true that this formulation does not -- a truly unexpected result or a significantly superior -- obviously superior result in the context of blending, it certainly shows a significant improvement across a variety of -- and the fact that this formulation has an improved result in at least one, and that result was unexpected, it should be sufficient to support the patentability of the product.

JUDGE LINCK: What -- go ahead, Lora.

JUDGE GREEN: Oh, I'm sorry. Do you have any discussion in your specification as to the criticality of these particular concentrations?

MS. ELMORE: Unfortunately, no, it's a generic discussion of the improvement --

JUDGE GREEN: Okay.

MS. ELMORE: -- of the the application. We believe that that issue should not be failed to patentability, since it is a necessary and inherent property of the formulation.

JUDGE GREEN: But one you wouldn't have gotten from this specification?

MS. ELMORE: You would not derive -- the specification was not -- is not actual disclosed. And to be honest, the results would show this unexpected result wasn't appreciated at the time the patent application filed.

JUDGE GREEN: Okay. So you don't even have a discussion of the crash-out times in your specification?

MS. ELMORE: No.

JUDGE GREEN: Okay. I just want to look at Figure 2 very quickly, which is your graph. It looks like you have data points at 25 percent, but you haven't presented any data at 25 percent. I mean, is that -- are those actual data points on there or --

MS. ELMORE: Those are actual data -- yes, those are actual data points. I didn't include them on the graph -- on the table -- for the purposes of -- it didn't provide me with a good comparison.

JUDGE GREEN: Well, it wasn't in -- from my recollection, it's not in the declaration anywhere except for this particular table.

MS. ELMORE: That's correct.

JUDGE GREEN: Okay. And then, looking at those lines, if I were to follow those lines across as I was doing this data, those are pretty much where I would expect the next points to follow, except for maybe the 30 percent at -- the 30 percent insulin at 15 grams per liter. That's the only one that seems to jump.

MS. ELMORE: Which is why, when I was discussing this data and these figures with my colleagues, we came to the conclusion that the particular figures didn't accurately display what was unexpected to result. It is true that if you increase the amount of a soluble component, a water-soluble component such as insulin, and decrease the amount of the water in a

soluble component such as DPPC, that you would expect the crash-out time of that resulting formulation to improve. So that fundamental question of where would you expect the trends to go is accurate. You would expect that the lower the solubility or the fewer amounts of solutes that you put in solution would improve crash-out time, and that by increasing the relative amount of protein, you would improve crash-out time.

What was unexpected, though, is that -- is that the property that was actually observed in this case went far beyond what was the expected result. You would not expect that by -- that you could prevent DPPC from crashing out by merely increasing the amount of insulin; that the insulin would have a protecting function in crash-out. Again, I refer to, in the table, A-4 and --

JUDGE GREEN: No, I understand the table. It's Figure 2 that I find to be interesting, because these seem to be normal experiments that anybody who was to perform this invention would do to figure out how these two components would interact with each other.

MS. ELMORE: Um-hum.

JUDGE GREEN: And I mean, it's pretty predictable where the next line on the plot is going to go. Once you have the first couple of data points, it seems to be pretty predictable, based on the experimentation a normal person in this art would do.

MS. ELMORE: Well -- but one of ordinary -- you're right. One of ordinary skill in the art would be motivated to identify an optimum concentration of the solution or spray time, and the context of performing these experiments was done with that in mind. However, it's my opinion that it requires a hindsight view of construction to say, well, if you

performed the first couple of experiments, which isn't caught in the prior art, that you would predict where the future prior art is going to go.

And in this particular situation, one would not have predicted that you could delay the crash-out time in a formulation which contained 12 grams per liter of DPPC by further increasing the amount of insulin. We didn't merely reduce the amount of DPPC and increase the amount of insulin to prevent crash-out. We added more insulin and that is an unexpected result. Even if, by looking at the figure, you could say, okay, if I increase the amount of insulin to 40 percent, you know, maybe I would delay crash-out even further. So the mere fact that the --

JUDGE GREEN: So what you're trying to argue as unexpected is the protective property of the insulin in keeping the -- I'm going to say it wrong -- the DPPC in solution?

MS. ELMORE: Correct.

JUDGE GREEN: Okay.

MS. ELMORE: That's correct.

JUDGE LINCK: Can you tell us the standard deviation for these data points?

MS. ELMORE: No, I cannot.

JUDGE LINCK: Was more than one experiment run at each?

MS. ELMORE: I believe that it was. I didn't ask -- clarify specific questions. These experiments were done in the context of identifying what the process was going to be for running clinical trial experiments, so I am confident that they were done seriously and are reliable --

JUDGE LINCK: It's just very difficult to give them weight without understanding what the standard deviation is.

(Pause.)

JUDGE ADAMS: That's all your arguments on that case?

MS. ELMORE: That's my argument.

JUDGE ADAMS: Any further questions from the Board?

JUDGE GREEN: No.

JUDGE ADAMS: Any questions?

JUDGE LINCK: No.

(Whereupon, the proceedings concluded.)